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CASE REPORT

Freeman–Sheldon syndrome with respiratory failure: A case report

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Summary
The Freeman–Sheldon syndrome is a rare congenital dysplasia principally characterised by facial and skeletal abnormalities secondary to a generalised myopathy. Thoracic scoliosis and facial abnormalities are the important features of this disease, and if left untreated, these can cause complications such as respiratory failure. We present the case of a 12-year-old girl with recurrent episodes of breathlessness who eventually presented with established cor pulmonale as a result of chronic respiratory failure. We hope that by presenting this case we can raise awareness of the possibility of extra-pulmonary restriction causing the patient's symptoms when physicians are presented with similar clinical scenarios.

Introduction

The Freeman–Sheldon[1] syndrome is a rare congenital dysplasia principally characterised by facial and skeletal abnormalities secondary to a generalised myopathy. Although more than 50 cases have now been described this syndrome has recently attracted attention in the anaesthetic literature. Patients with the syndrome may present anaesthetic problems involving difficulties with both intubation and intravenous access. We describe one child with the Freeman–Sheldon syndrome who presented with respiratory failure. The syndrome may be diagnosed by the clinical examination of an affected newborn infant. Not all of the features described are necessarily present in a single patient. The increased tone and fibrosis of the facial muscles gives rise to an immobile mask-like facial expression. In addition to hypertelorism, the eyes are deeply set below a supraorbital ridge with blepharophimosis and ptosis. Other eye features which may be present are epicanthic folds and strabismus. The nose is small and the alae nasi are hypoplastic. The myopathic fibrotic circumoral musculature results in microstomia with the characteristic protruding pursed ''whistling'' lips and a prominent long philtrum. The contracted facial musculature and soft tissues produce a lingually directed force on the lower teeth, which in turn pushes the lower incisors lingually and leads to an unusual modelling of the chin. Externally there is a mound of subcutaneous tissue inferior

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to the lower lip and demarcated by vertical furrows on either side.

Mandibular development may also be abnormal with small mandibular bodies of the rami. The high arched palate, small tongue and limited palatal movement eventually result in a nasal quality of speech. The overall appearance of the skull is often dolichocephalic. Muscle contractures result in the development of a relatively short neck and high (cephalad) positioning of the larynx. The generalised myopathy is associated with the later development of kyphoscoliosis which, in addition to intercostal myopathy, can lead to restrictive lung disease. By affecting the oro- and nasopharyngeal muscles, the myopathy may produce chronic upper airway obstruction, most notably observed in infants.[9,10] Secondary to this, pulmonary hypertension may develop and should be sought specifically when evaluating these patients. There is an increased incidence of pectus excavatum and spina bifida occulta in this syndrome. The limbs are commonly involved by the myopathy and contracture deformities develop. In the upper limb, ulnar deviation of the wrist and flexion contractures of the fingers occur. In the lower limb, talipes equinovarus, vertical talus and contracted toes may be present. Difficulty with swallowing may lead to malnourishment and failure to thrive. Although overall growth may be retarded, eventual intelligence is usually in the normal range. The results of electromyography and muscle biopsy may support the diagnosis.[2,7] Most of the features of this syndrome remain into adulthood. Treatment consists of correcting malnutrition in the infant combined with corrective surgery in the child and adult for the wide range of musculoskeletal deformities. Formerly it was observed that improvement of the manifestations occurred on reaching adult age.[3] More recently Malkawi et al.[4] have suggested that early surgery, especially of the hand of the affected child, may improve the outcome of the deformities. Kyphoscoliosis, as in idiopathic scoliosis, develops with growth of the child and commonly present in the teenager when it may require surgical treatment. Microstomia remains into adulthood and, by reducing the oral aperture, presents difficulties to both the dentist and the anaesthetist. In most cases, early corrective surgery of the deformities can result in the patient leading a normal life with normal expectancy.

Case history

A 12-year-old girl presented to our ER with a one week history of lower limb swelling bilaterally and periorbital odema, associated with a mild cough and dyspnoea on exertion. She had been diagnosed as Freeman–Sheldon Syndrome at the age of one year on the basis of the 1996 classification [8] of distal arthrogryposis type 2A(DA2A). She had all the features of this rare genetic condition which include a small ''whistling'' mouth, flat mask-like face, club feet, joint contractures involving the feet and hands, as well as an S shaped scoliosis of her spine which had not been surgically corrected. She had been given the label of Asthmatic on the basis of recurrent bouts of dyspnoea which had resulted in several ER visits over the preceding 2 years but ER sheet notes commented that her symptoms never responded completely to bronchodilators, and recurrent presentations were attributed to poor compliance with prescribed anti asthmatic medication.

On examination she was mildly distressed, mildly tachypnoeic with respiratory rate 18 per minute, pulse 98 per minute regular, BP 118/68, afebrile, had cyanotic lips, a raised JVP at 6 cm above sternal angle, loud P2 on auscultation of heart sounds, decreased breath sounds globally with no wheeze. Abdominal examination revealed tender hepatomegaly with no ascites, and she had bilateral lower limb oedema grade 3. Oxygen saturations on room air were 80% and rose to 99% with 4 l/min oxygen supplementation.

Investigations in the Emergency Room: ABGs on 4 l O_2: pH 7.25, $PaCO_2$ 55, PaO_2 92, HCO_3 33.

CBC and renal panel normal.

Liver function: AST 446, ALT 448, Alb 29, bil 18, Alp 186, GGT 56.

BNP 4315, CK 53.

CXR: S shaped scoliosis with convexity to the right side of thoracic spine. Cardiac silhouette enlarged. No active parenchymal pathology.

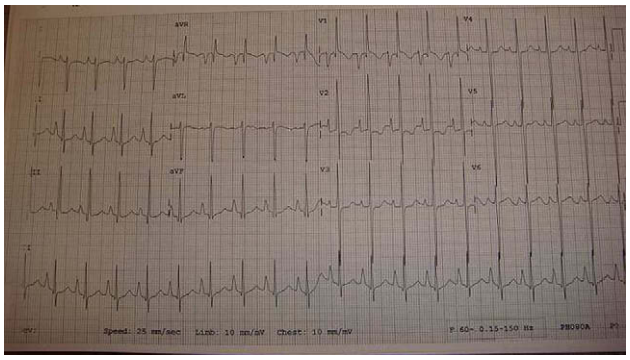
ECG: Right axis deviation, Right ventricular hypertrophy with strain pattern.

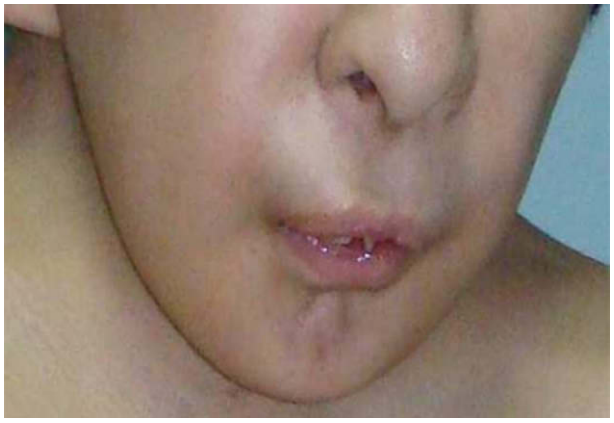
The clinical impression was of cor pulmonale secondary to chronic type 2 respiratory failure due to restrictive lung disease from severe thoracic scoliosis. The patient was commenced on non invasive ventilation in the form of BiPAP with initial IPAP 8 cm H_2O and EPAP 4 cm H_2O, gradually increased as tolerated by the patient up to 12/8. Also commenced on Furosemide 20 mg IV BID and further investigations were ordered.

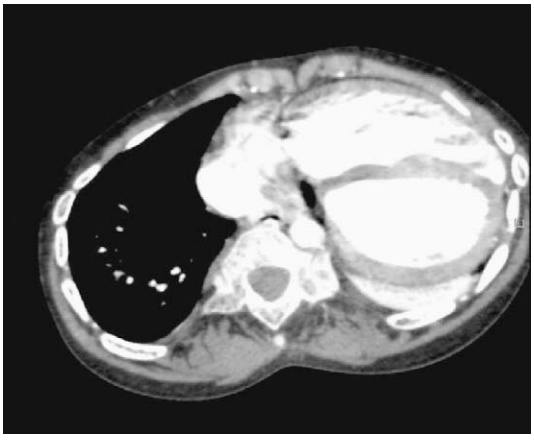
ECHO showed a squeezed very small D-shaped LV cavity secondary to RV pressure and volume overload. Normal LV systolic function. Giant RA and RV, hypertrabeculated, with severely impaired RV systolic and diastolic function. Tricuspid valve is normal in structure and function. Trivial TR with estimated PAP of 70 mm Hg. Dilated main pulmonary trunk and its branches with trivial PR and RVOT signal indicative of significant pulmonary hypertension.

Spiral CT showed no evidence of pulmonary embolism with no filling defect in the main pulmonary, segmental and subsegmental arteries, normal lung parenchyma. For the pulmonary hypertension nebulised Iloprost and Sildanefil were added to her treatment. Over the following few days the patient improved significantly. The oedema resolved gradually, and though she initially found NIV difficult to tolerate because of her facial structure, various interfaces were tried and she remained comfortable with the nasal swift pillow. She was discharged home on nocturnal BiPAP support only and on follow up she remained well with stable daytime ABGs.

Follow up ECHO 1 month after presentation showed normal LV size and function. No sign of pulmonary hypertension. RV/RA normal size. No D shape appearance and normal pulmonary flow. Iloprost and Sildanefil were discontinued and she maintains an active life attending school again and with a good level of activity. She is not on any medications for Asthma.







Discussion

Since its original description in 1938, Freeman—Sheldon syndrome has also been variously described as the Windmill-Vane-Hand syndrome,[5] cranio-carpo-tarsal dysplasia and the whistling face syndrome.[6,8] Although most cases occur sporadically it is thought to be transmitted by autosomal dominant inheritance[2] and there are at least two case reports of first degree transmission.[3,4] Not all cases are equally affected and there exists a spectrum of deformity

and disability. The precise mechanism of this combined skeletal and muscular dysplasia is unclear, although Sauk et al.[2] suggest that hypoplasia of muscle bundles supplied by the motor branch of major nerves may cause these abnormalities. Biopsy of the affected muscles reveals fibrosis which may contribute to the contractures. The presence of facial deformities and thoracic Scoliosis are well known causes of respiratory failure and the use of non invasive ventilatory support offers significant morbidity and mortality benefit. The progression of the kyphoscoliosis curve can be slowed through bracing but surgery is required in most cases. We present a case of an unfortunate patient who developed respiratory failure at a young age as a complication from this condition. To our knowledge this is the first reported case of Freeman—Sheldon Syndrome presenting with chronic respiratory failure necessitating non invasive ventilatory support at such a young age. We feel that the possibility of restrictive lung disease causing her symptoms of dyspnoea were overlooked prior to her eventual presentation with cor pulmonale, and the diagnosis of Asthma was probably erroneous in her case Junior doctors faced with a breathless patient should be clinically aware and entertain the possibility of extra-pulmonary restriction causing the patient's symptoms in the appropriate clinical setting.

In conclusion: We hope that the reporting of this case will help to raise awareness of the problems associated with this syndrome such as respiratory failure.

Conflict of interest statement

None of the authors have any conflict of interest to disclose. We have not received anything of value from a commercial or other party related directly or indirectly to the subject of this case report.

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